### PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER	coo Form POT/ICA/000	
INGN:120WO	See Form PCT/ISA/220 as well as, where applicable, item 5 below.		
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)	
PCT/US2005/006108	24/02/2005	24/02/2004	
Applicant			
INTROGEN THERAPEUTICS, INC	· · · · · · · · · · · · · · · · · · ·		
This International Search Report has beer according to Article 18. A copy is being tra	n prepared by this International Searching Auth ansmitted to the International Bureau.	nority and is transmitted to the applicant	
This International Search Report consists	of a total of sheets.		
X It is also accompanied by	a copy of each prior art document cited in this	report.	
Basis of the report     a. With regard to the language, the language in which it was filed, unle	international search was carried out on the bas ess otherwise indicated under this item.	sis of the international application in the	
The international of this Authority (Rul	search was carried out on the basis of a transk le 23.1(b)).	ation of the international application furnished to	
b. With regard to any <b>nucleo</b>	otide and/or amino acid sequence disclosed i	in the international application, see Box No. I.	
2. X Certain claims were four	nd unsearchable (See Box II).		
3. Unity of invention is lack	king (see Box III).		
4. With regard to the title,			
the text is approved as sul			
· · · · · · · · · · · · · · · · · · ·	hed by this Authority to read as follows:		
COMBINATION OF AD-P53	AND CHEMOTHERAPY FOR THE TRI	EATMENT OF TUMOURS	
5. With regard to the abstract,			
X the text is approved as sub	omitted by the applicant.		
the text has been establish may, within one month from	hed, according to Rule 38.2(b), by this Authority m the date of mailing of this international searc	y as it appears in Box No. IV. The applicant the report, submit comments to this Authority.	
6. With regard to the drawings,			
a. the figure of the <b>drawings</b> to be pu	ublished with the abstract is Figure No.		
as suggested by the	, ,		
	s Authority, because the applicant failed to sugg		
	s Authority, because this figure better character	izes the invention.	
b. A Hone of the rightes is to be	e published with the abstract.		

International Application No PCT/US2005/006108

		101/002003/000100
A. CLASSI IPC 7	FICATION OF SUBJECT MATTER A61K48/00 A61K38/17 A61P35/0	
According to	b International Patent Classification (IPC) or to both national classifica	ation and IPC
B. FIELDS	SEARCHED	
Minimum do IPC 7	cumentation searched (classification system followed by classification ${\tt C12N-A61K}$	on symbols)
	ion searched other than minimum documentation to the extent that s	
	ata base consulted during the international search (name of data base	· · · · · · · · · · · · · · · · · · ·
EPO-In	ternal, BIOSIS, WPI Data, PAJ, EMBAS	5E
C. DOCUME	ENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the rele	evant passages Relevant to claim No.
<b>X</b>	NEMUNAITIS J ET AL: "Adenovirus-p53 gene transfer in sequence wit cisplatin to tumors of patients wonn-small-cell lung cancer" JOURNAL OF CLINICAL ONCOLOGY, vol. 18, no. 3, February 2000 (20 pages 609-622, XP002331130 ISSN: 0732-183X page 610, left-hand column, paragright-hand column, paragright-hand column, paragraph 1 page 611, left-hand column, paragpage 612, right-hand column, paragpage 609 abstract	th vith 100-02), graph 5 -
X Furti	ner documents are listed in the continuation of box C.	Patent family members are listed in annex.
<ul> <li>Special categories of cited documents:</li> <li>A document defining the general state of the art which is not considered to be of particular relevance</li> <li>E earlier document but published on or after the international filing date</li> <li>T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to</li> </ul>		
*L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  *O* document referring to an oral disclosure, use, exhibition or other means  *P* document published prior to the international filing date but  involve an inventive step when the document is taken alone when the document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such document, such combination being obvious to a person skilled in the art.		
	ant published prior to the international filing date but an the priority date claimed	*&* document member of the same patent family
	actual completion of the international search	Date of mailing of the international search report
	2 June 2005	04/08/2005
Name and r	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Sitch, W

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International Application No
PCT/US2005/006108

COntinu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/US2005/006108
ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
		nelevant to claim No.
X	BULLER RICHARD E ET AL: "Long term follow-up of patients with recurrent ovarian cancer after Ad p53 gene replacement with SCH 58500" CANCER GENE THERAPY, vol. 9, no. 7, July 2002 (2002-07), pages 567-572, XP002331131 ISSN: 0929-1903 page 568, left-hand column, paragraph 1 - page 569, left-hand column, paragraph 1	1-30
<b>X</b>	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1997, PIROLLO KATHLEEN F ET AL: "P53 mediated sensitization of squamous cell carcinoma of the head and neck to radiotherapy" XP002331134 Database accession no. PREV199799548911 abstract & ONCOGENE, vol. 14, no. 14, 1997, pages 1735-1746, ISSN: 0950-9232	1-35
X	DATABASE BIOSIS 'Online! BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1997, CHANG ESTHER H ET AL: "Restoration of the G-1 checkpoint and the apoptotic pathway mediated by wild-type p53 sensitizes squamous cell carcinoma of the head and neck to radiotherapy" XP002331135 Database accession no. PREV199799596956 abstract & ARCHIVES OF OTOLARYNGOLOGY HEAD AND NECK SURGERY, vol. 123, no. 5, 1997, pages 507-512, ISSN: 0886-4470 /	1-35

International Application No
PCT/US2005/006108

0.40	ALL NOOLUITATIO CONCENTRATION OF THE PROPERTY	PC1/US2005/006108	
C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages		
Odlegory	Official of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
X	GURNANI MAYA ET AL: "Adenovirus-mediated p53 gene therapy has greater efficacy when combined with chemotherapy against human head and neck, ovarian, prostate, and breast cancer"  CANCER CHEMOTHERAPY AND PHARMACOLOGY, vol. 44, no. 2, August 1999 (1999-08), pages 143-151, XP002331132  ISSN: 0344-5704  page 143  abstract  page 144, right-hand column, paragraph 1  page 145, right-hand column, paragraph 4  page 147, right-hand column, paragraph 4  page 148, right-hand column, paragraph 1  page 148, right-hand column, paragraph 1	1-35	
X	NIELSEN L L ET AL: "ADENOVIRUS-MEDIATED P53 GENE THERAPY AND PACLITAXEL HAVE SYNERGISTIC EFFICACY IN MODELS OF HUMAN HEAD AND NECK, OVARIAN, PROSTATE AND BREAST CANCER" CLINICAL CANCER RESEARCH, THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, US, vol. 4, no. 4, April 1998 (1998-04), pages 835-846, XP002331133 ISSN: 1078-0432 page 835 abstract page 837, left-hand column, last paragraph right-hand column, paragraph 1 page 843; figures 6,7	1-35	
X	ALEXANDER W A ET AL: "Tumor-targeted sensitization to chemotherapy by systemically delivered ligand mediated wtp53 gene therapy" PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL MEETING, vol. 40, March 1999 (1999-03), page 596, XP001206623 & 90TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH; PHILADELPHIA, PENNSYLVANIA, USA; APRIL 10-14, 1999 ISSN: 0197-016X abstract #3930	1-35	

2

International application No. PCT/US2005/006108

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)	
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:	
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:	
Although claims 1-30 are directed to a method of treatment of the human/anima body, the search has been carried out and based on the alleged effects of the compound/composition.	. 1 !
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:	
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).	
Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)	
This International Searching Authority found multiple inventions in this international application, as follows:	
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.	
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.	
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:	
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:	
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.	

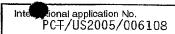
Internation No PCT/US2005/006108

A CLASS	VEIQATION OF OUR		PC1/US2005/006108
ÎPC 7	BIFICATION OF SUBJECT MATTER A61K48/00 A61K38/17 A61P35	/00	
According t	to International Patent Classification (IPC) or to both national class	ification and IPC	
B. FIELDS	SEARCHED		
176 /	ocumentation searched (classification system followed by classific C12N A61K	- ,	
	ition searched other than minimum documentation to the extent that the standard of the consulted during the international search (name of data		
	ternal, BIOSIS, WPI Data, PAJ, EMBA		earch terms used)
	ENTS CONSIDERED TO BE RELEVANT		
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X Furth	er documents are listed in the continuation of box C.	- Database in	
<u></u>	,	Latent raminy mem	nbers are listed in annex.
"A" documer conside "E" earlier do filing da		cited to understand the invention  "X" document of particular	ed after the international filing date t in conflict with the application but e principle or theory underlying the relevance; the claimed invention
citation	nt which may throw doubts on priority claim(s) or s cited to establish the publication date of another or other special reason (as specified) nt referring to an oral disclosure, use, exhibition or leans	"Y" document of particular in cannot be considered document is combined	novel or cannot be considered to ep when the document is taken alone relevance; the claimed invention to involve an inventive step when the with one or more other such docu-
ialei ilia	nt published prior to the international filing date but an the priority date claimed	in the art.  "&" document member of the	ion being obvious to a person skilled
Date of the a	ctual completion of the international search		nternational search report
22	2 June 2005	04/08/200!	5
Name and ma	ailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk	Authorized officer	
	Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Sitch, W	

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Internation I Application No PCT/US2005/006108

		PC1/US200	
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Remark on Protest The additional search fees were accompanied by the applicant's protest.
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